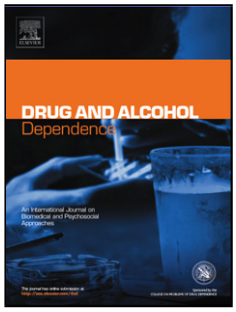
Journal Pre-proof



Association of prenatal alcohol exposure with preadolescent alcohol sipping in the ABCD study

Briana Lees, Louise Mewton, Lexine A. Stapinski, Maree Teesson, Lindsay M. Squeglia

PII: S0376-8716(20)30352-5

DOI: https://doi.org/10.1016/j.drugalcdep.2020.108187

Reference: DAD 108187

To appear in: *Drug and Alcohol Dependence*

Received Date: 9 June 2020

Revised Date: 30 June 2020

Accepted Date: 14 July 2020

Please cite this article as: { doi: https://doi.org/

Association of prenatal alcohol exposure with preadolescent alcohol sipping in the ABCD Study

Briana Lees,[1] Louise Mewton,[2] Lexine A. Stapinski,[1] Maree Teesson,[1] Lindsay M. Squeglia[3]

[1]The Matilda Centre for Research in Mental Health and Substance Use, University of Sydney

[2]Centre for Healthy Brain Ageing, University of New South Wales

[3] Department of Psychiatry and Behavioral Sciences, Medical University of South Carolina

Corresponding Author: Briana Lees, B. Psych (Hons), Level 6 Jane Foss Russell Building G02, Camperdown, NSW 2006. Phone: +61 2 8627 9021. Email: briana.lees@sydney.edu.au

Word Count: 2,203

Tables / Figures: 2

Highlights

- Any prenatal alcohol exposure increased risk of alcohol experimentation by ages 9-10
- Linear association found for levels of exposure and likelihood of sipping alcohol
- Results were consistent when adjusting for known confounding factors
- Prenatal alcohol exposure is a modifiable risk factor for early alcohol use

Abstract [<250]

Background: Early alcohol use initiation is one of the strongest predictors of alcohol use disorders. Identifying modifiable risk factors for problematic alcohol use can guide prevention initiatives. Globally, approximately 10% of women consume alcohol during pregnancy, however the impact of prenatal alcohol exposure (PAE) on offspring alcohol use patterns has been understudied. The aim of this study was to examine associations between PAE and preadolescent alcohol use behaviors.

Methods: Cross-sectional data were utilized from 10,119 children aged 9.0 to 10.9 years (M=9.9, SD=0.6) enrolled in the Adolescent Brain Cognitive Development Study, based in the United States. Linear mixed models tested associations between PAE and endorsement of non-religious alcohol sipping in offspring, when adjusting for confounding factors.

Results: In total, 2,675 (26.4%) youth were prenatally exposed to alcohol. Among PAE youth, total standard drinks consumed during pregnancy ranged from 0.4 to 90 drinks (M=26.8, SD=24.5). Compared to unexposed youth, those with any alcohol exposure during early pregnancy (~0-7 weeks) were 1.7 times (95% CI 1.4-2.0, $p < .0001$) more likely to endorse sipping alcohol by ages 9 to 10, while youth with low-level doses of alcohol throughout the entire pregnancy were 2.9 times (95% CI 1.9-4.6, $p < .0001$) as likely to endorse sipping, when adjusting for confounding factors. A dose-dependent association between total standard drinks consumed during pregnancy and youth sipping endorsement was observed.

Conclusions: This study shows that any alcohol use during pregnancy may play an important role in very early alcohol use experimentation among offspring by ages 9-10.

Keywords: alcohol; pregnancy; children

Introduction

Globally, one in 10 women consume alcohol during pregnancy, and of these women, ~90% consume low levels where offspring do not meet criteria for fetal alcohol spectrum disorders (Popova et al., 2017). Recently, we showed that relatively low-level prenatal alcohol exposure (i.e., 1-80 standard drinks consumed during pregnancy) was associated with early childhood externalizing problems, impulsiveness, attention deficits, aggression and neurobehavioral aberrations (Lees et al., in press). Despite these behaviors being established correlates of early alcohol initiation and escalation (Meque et al., 2019, Groenman et al., 2017, Erskine et al., 2016, Lees et al., 2019), the impact of prenatal alcohol exposure (PAE) on offspring alcohol use patterns are relatively understudied.

Previous research has focused on the effects of frequent, heavy alcohol use during pregnancy. Baer et al. (2003) reported that exposure to five or more drinks per occasion was associated with alcohol problems in offspring at age 21. Alati et al. (2006) found that exposure to three or more drinks per occasion increased the odds of alcohol use disorders at age 21, compared to no or low levels of PAE. Likewise, Goldschmidt et al. (2019) reported that prenatal exposure to one or more drinks per day was linearly associated with increased odds of reporting symptoms of alcohol use disorders at age 22. Two studies drawing on the adolescent cohort (10-16 years) from the Maternal Health Practices and Child Development Project examined youth exposed to daily alcohol use, either in the first trimester only or throughout the entire pregnancy (Cornelius et al., 2016a, Cornelius et al., 2016b). First trimester PAE was associated with higher levels of drinking in adolescence (Cornelius et al., 2016a), and exposure to more than one drink per day throughout pregnancy was associated with persistent adolescent drinking (Cornelius et al., 2016b). In summary, heavy and frequent exposure to alcohol in utero has been associated with increased odds of offspring alcohol use and related problems in adolescence and young adulthood.

To our knowledge, no studies have explored associations between offspring alcohol use and low-level PAE which is more typical of the general population (Popova et al., 2017). There has also

been very little attention given to the impact of PAE on early alcohol experimentation in preadolescents. Earlier age of alcohol use initiation is one of the strongest predictors of a lifetime diagnosis of alcohol use disorder, and predicts a more severe chronic course of use throughout adolescence and adulthood (Grant and Dawson, 1997, Guttmannova et al., 2011). Therefore, it is critical that associations between PAE and early alcohol use behaviors are explored to progress knowledge of potentially modifiable risk factors for problematic alcohol use in young people. To fill these important gaps in the literature, the current study examined associations between lower-level PAE and lifetime report of alcohol experimentation in 10,119 children aged 9 to 10 years from the Adolescent Brain Cognitive Development (ABCD) Study. It was hypothesized that PAE youth would be at higher odds of endorsing alcohol experimentation by ages 9 to 10 than unexposed youth, controlling for demographic and socioenvironmental variables.

Methods

Participants

The ABCD Study release 2.0.1 contains cross-sectional baseline data from 11,875 children aged 9.0 to 10.9 years and their parent. A probability sample was recruited through schools proximal to the 21 research sites across the United States (Hagler et al., 2019). Informed consent and assent were obtained from a parent or legal guardian and the child, respectively. Procedures were approved by a central Institutional Review Board. Of the 11,875 participants enrolled, 1,756 were removed from the current analysis because of incomplete data (n=10,119).

Outcome Measure

The iSay Sip Inventory (Jackson et al., 2015) assessed youth-reported sipping endorsement via the question "*have you ever had alcohol not as part of a religious ceremony?*". While the number of sipping occasions were assessed, data were positively skewed with little gradation (M=2.3, SD=1.4, max=15), therefore, the outcome was examined as a dichotomous (y/n) rather than continuous measure. The majority of youth sipped from their parent's drink (79.5%), with one in four

(26.3%) doing so while their parent wasn't looking. Very few youth had consumed a full drink of alcohol (n=21) or tried tobacco (n=81) or cannabis (n=12).

Explanatory Measures

Prenatal alcohol exposure (parent report)

Retrospective report of maternal alcohol use before and after knowledge of pregnancy was assessed via the modified Developmental History Questionnaire (Merikangas et al., 2009, Kessler et al., 2009). From the available data, three PAE measures were derived (for details, see Lees et al., in press): (1) a dichotomous variable capturing any exposure (n=10,119); (2) a categorical PAE variable of common patterns of drinking (n=9,091); and (3) a continuous estimate of total standard drinks consumed during pregnancy, following 1.5% winsorization to convert outliers (n=9,180). To categorize youth into common alcohol exposure patterns, maternal drinking was categorized into abstinent (< 1 standard drink/occasion throughout pregnancy), light (1-2 drinks/occasion, <7 drinks/week), moderate (3-4/occasion, <7/week), heavy (<5/occasion, 7+/week), or binge drinking (5+/occasion) before and after knowing of pregnancy (O'Leary et al., 2010). Common patterns were identified: (1) abstinent throughout pregnancy, (2) low-level use during early pregnancy (light before knowing, abstinent after knowing of pregnancy), (3) heavier-level use during early pregnancy (moderate, heavy, and binge drinkers before knowing, abstinent or light drinking after knowing), (4) low-level use throughout pregnancy. Further details and relevant questions from the ABCD protocol are described elsewhere (Lees et al., in press).

Covariates (youth and parent report)

The following fixed effects were included in all statistical models and were dummy coded: sex (M/F), race/ethnicity (White, Black, Hispanic, Asian, Other), parent education (<high school diploma, high school diploma or equivalent, college, Bachelor's degree, Postgraduate degree), household income (<50K, 50-100K, >100K), and marital status (single parent household, married). Youth age was included as a continuous fixed effect.

Other potentially confounding parent-reported dummy coded variables were examined: prenatal tobacco, cannabis, heroin, or cocaine exposure (y/n), maternal depression (y/n), youth alcohol access (easy, hard, unknown), and past/present parental alcohol problems (y/n; e.g., alcohol-related marital separation or family problems, fired from work, arrests or DUIs, health problems, alcohol treatment program). In addition, birthweight, gestational age, maternal age, and youth-reported parental monitoring were explored as potentially confounding continuous covariates.

Analysis

Linear mixed-effects models, fitted using maximum likelihood estimation, were used with random effects for family nested within research site (R package: 'glmmTMB'). Analyses examined the association between the three PAE variables and youth sipping endorsement. For each analysis, three statistical models were compared using the ANOVA function and Bayesian Information Criterion: (1) socio-demographic variables only (i.e., sex, age, race/ethnicity, parent education, marital status, household income), (2) PAE and fixed-effect socio-demographic covariates, (3) PAE, socio-demographic, and other potentially confounding fixed-effect covariates (i.e., prenatal tobacco, cannabis, heroin, or cocaine exposure, parental alcohol problems, birthweight, gestational age, maternal age, maternal depression, parent monitoring, youth alcohol access). For the patterns of exposure analysis, week of pregnancy knowledge (M=6.9, SD=6.7) was entered as an additional fixed-effect covariate in models 2 and 3. While PAE findings from models 2 and 3 were consistent, model 2 was the best fit to the data and used in the final analysis, reported herein. Of the potentially confounding fixed-effect covariates included in model 3, prenatal heroin exposure (n=16), low parent monitoring, and easier alcohol access were significantly associated with increased odds of offspring sipping endorsement. Considering these associations, post-hoc analysis examined possible interactions between PAE with parent monitoring and youth alcohol access. Sensitivity analyses examined whether associations remained when youth with prenatal tobacco or other drug exposure (n=1,367), and/or parental history of alcohol problems (n=1,381) were excluded, and remaining PAE and unexposed youth were demographically matched 1:1 on covariates that significantly differed

between groups (i.e., race/ethnicity, parent education, household income; R package: 'MatchIt'). The more homogenous subsample included 3,122 youth (50.0% PAE).

Results

Of 10,119 youth included in the analyses, 2,675 (26.4%) were prenatally exposed to alcohol (Table). Among those with PAE, total standard drinks consumed during pregnancy ranged from 0.4 to 90.0 drinks (M=26.8, SD=24.5), following outlier conversion. Compared to unexposed youth, the fully adjusted odds ratio (aOR) of sipping endorsement was 1.7 (95% CI = 1.5 to 1.9, $p < 2e\text{-}16$) for those exposed to any alcohol in utero. When exploring common patterns of alcohol exposure, the aOR was 1.7 (95% CI = 1.4 to 2.0, $p = 7.9e\text{-}11$) for those exposed to low-level doses of alcohol during early pregnancy only, 1.7 (95% CI = 1.4 to 2.0, $p = 1.3e\text{-}07$) for those exposed to heavier-level doses of alcohol during early pregnancy only, and 2.9 (95% CI = 1.9 to 4.6, $p = 3.5e\text{-}06$) for those exposed to low-level doses of alcohol throughout pregnancy (Figure). A dose-dependent association between total standard drinks consumed during pregnancy and youth sipping endorsement was observed ($\beta = 0.2$, $SE = 0.03$, $Z = 5.8$, $p = 7.3e\text{-}09$).

Other significant correlates of sipping endorsement by age 9 to 10 years included male sex (adjusted odds ratio [AOR] = 1.3, 95% CI = 1.1 to 1.4, $p = .0001$), older age (AOR = 1.2, 95% CI = 1.1 to 1.3, $p = 7.6e\text{-}05$), highly educated (>Bachelor) parents (AOR = 1.5, 95% CI = 1.2 to 1.1.9, $p = .002$), and high household income (AOR = 1.3, 95% CI = 1.0 to 1.6, $p = .04$), see Figure. Compared to White youth, Black youth were less likely to endorse lifetime alcohol sipping (AOR = 0.6, 95% CI = 0.4 to 0.7, $p = 3.2e\text{-}06$).

Interactions between PAE and parent monitoring, and youth alcohol access were not significantly associated with sipping endorsement. Sensitivity analyses confirmed that all findings were consistent when excluding those with prenatal tobacco or other drug exposure, and/or parental history of alcohol problems and demographically matching 3,122 remaining youth.

Discussion

This study is the first to show that low-level alcohol use during any stage of pregnancy is associated with increased odds of offspring's early (age 9-10) alcohol use. This association remained significant after controlling for potentially confounding factors, and during stringent demographic matching procedures which excluded youth with prenatal tobacco or other drug exposure, or parental history of alcohol problems.

The results add to the small body of literature on the impact of PAE on offspring alcohol use behaviors in adolescence (Cornelius et al., 2016a, Cornelius et al., 2016b) and young adulthood (Baer et al., 2003, Alati et al., 2006, Goldschmidt et al., 2019). Taken together, these studies demonstrate continuity of risk related to PAE from preadolescent alcohol experimentation, to adolescent high and chronic drinking, and early onset alcohol problems and alcohol use disorders in young adulthood.

Several factors may be contributing to associations between PAE and offspring alcohol use behaviors, including sociocultural, neurobiological, and genetic influences. It is well established that factors such as parental rules, parental alcohol use, and availability of substances are risk factors of early alcohol use behaviors (Simons-Morton et al., 2001). While parental monitoring and accessibility of alcohol use were related to youth alcohol experimentation in the current study, potential moderating effects with PAE were not observed. This indicates that these relationships are not significantly inter-related and may suggest that PAE and sociocultural factors relate to alcohol use through differing mechanisms. For example, our prior research revealed dose-dependent alcohol-associated brain differences in youth with PAE, which partially explained later externalizing problems (Lees et al., in press). Future longitudinal studies should explore whether alcohol-associated changes in the fetal brain are also contributing to alcohol use behaviors. It has been suggested that PAE may selectively enhance the pleasantness and emotional reactivity of alcohol odor and taste in offspring, and this may contribute to greater escalation in drinking behaviors (Hannigan et al., 2015, Anunziata et al., 2020). Genetic associations between parental and offspring alcohol use patterns are also a

possibility. The current study did not observe a significant association between parental history of alcohol problems and endorsement of alcohol sipping in offspring. However, associations with non-problematic parental alcohol use behaviors or parental alcohol use patterns during the child's lifespan were not explored and may show different results. Further research is needed to improve understanding of how maternal drinking during pregnancy confers risk to offspring alcohol use to better inform prevention and intervention strategies.

Key strengths of this study include the large, diverse sample of youth which allowed for robust estimates and detailed characterization of the relationship between PAE and offspring alcohol experimentation. Additionally, it is the first study in this field to examine the effects of PAE where levels of exposure are more reflective of the general population (Popova et al., 2017). Furthermore, using a mixed model analytic approach allowed for appropriate adjustment of the complexity of factors that influence youth behaviors. Study limitations include: (1) potential maternal underreporting of alcohol use during pregnancy, (2) imprecise retrospective data on exposure patterns, (3) absence of data on trimester-specific exposure, (4) lack of data on non-problematic parental alcohol use behaviors, (5) ~20% missing data for patterns of PAE, and (6) utilization of a probability sample which is not necessarily representative of the US population. Additionally, the influence of paternal contribution to offspring behavior was not examined and should be examined alongside PAE in future studies.

In conclusion, this study shows that any alcohol use during any stage of pregnancy may play an important role in very early alcohol use experimentation among offspring by ages 9-10.

Contributors:

All authors are responsible for this reported research. Lees and Squeglia conceptualized the study. Lees conducted the analyses and drafted the manuscript. All authors interpreted results and critically reviewed and revised the manuscript. All authors approved the final manuscript.

Funding and Acknowledgements:

Salary support was provided by the Australian National Health and Medical Research Council (GNT1169377 to BL; GNT1132853 to LAS; GNT1041756 and GNT1078407 to MT) and National Institute on Drug Abuse (U01 DA041093 to LMS). The content is solely the responsibility of the authors and does not necessarily represent the official views of the Australian National Health and Medical Research Council or National Institute on Drug Abuse.

Disclaimer:

Data used in the preparation of this article were obtained from the Adolescent Brain Cognitive Development (ABCD) Study (https://abcdstudy.org), held in the NIMH Data Archive (NDA). This is a multisite, longitudinal study designed to recruit more than 10,000 children aged 9-10 and follow them over 10 years into early adulthood. The ABCD Study is supported by the National Institutes of Health and additional federal partners “under award numbers U01DA041022, U01DA041028, U01DA041048, U01DA041089, U01DA041106, U01DA041117, U01DA041120, U01DA041134, U01DA041148, U01DA041156, U01DA041174, U24DA041123, and U24DA041147”. A full list of supporters is available at https://abcdstudy.org/nih-collaborators. A listing of participating sites and a complete listing of the study investigators can be found at https://abcdstudy.org/principal-investigators.html. ABCD consortium investigators designed and implemented the study and/or provided data but did not necessarily participate in analysis or writing of this report. This manuscript reflects the views of the authors and may not reflect the opinions or views of the NIH or ABCD consortium investigators. The ABCD data repository grows and changes over time. The ABCD data used in this report came from the curated annual release 2.0.1.

Declaration of interest: The authors declare no conflict of interest.

References

ALATI, R., AL MAMUN, A., WILLIAMS, G. M., O'CALLAGHAN, M., NAJMAN, J. M. & BOR, W. 2006. In utero alcohol exposure and prediction of alcohol disorders in early adulthood: a birth cohort study. *Arch Gen Psychiatry,* 63**,** 1009-16.

ANUNZIATA, F., MACCHIONE, A. F., MITRANO, A. S., D'ALOISIO, G., FERREYRA, M. E., PONTORIERO, R. D., AHUMADA, L. A. & MOLINA, J. C. 2020. Respiratory and emotional reactivity to ethanol odor in human neonates is dependent upon maternal drinking patterns during pregnancy. *Drug and Alcohol Dependence,* 213**,** 108100.

BAER, J. S., SAMPSON, P. D., BARR, H. M., CONNOR, P. D. & STREISSGUTH, A. P. 2003. A 21-Year Longitudinal Analysis of the Effects of Prenatal Alcohol Exposure on Young Adult Drinking. *Archives of General Psychiatry,* 60**,** 377-385.

CORNELIUS, M. D., DE GENNA, N., GOLDSCHMIDT, L., LARKBY, C. & DAY, N. 2016a. Adverse Environmental Exposures During Gestation and Childhood: Predictors of Adolescent Drinking. *Subst Use Misuse,* 51**,** 1253-63.

CORNELIUS, M. D., GOLDSCHMIDT, L. & DAY, N. L. 2016b. Gestational Alcohol Exposure and Other Factors Associated With Continued Teenage Drinking. *Health Educ Behav,* 43**,** 428-33.

ERSKINE, H. E., NORMAN, R. E., FERRARI, A. J., CHAN, G. C. K., COPELAND, W. E., WHITEFORD, H. A. & SCOTT, J. G. 2016. Long-Term Outcomes of Attention-Deficit/Hyperactivity Disorder and Conduct Disorder: A Systematic Review and Meta-Analysis. *Journal of the American Academy of Child & Adolescent Psychiatry,* 55**,** 841-850.

GOLDSCHMIDT, L., RICHARDSON, G. A., DE GENNA, N. M., CORNELIUS, M. D. & DAY, N. L. 2019. Prenatal alcohol exposure and offspring alcohol use and misuse at 22 years of age: A prospective longitudinal study. *Neurotoxicol Teratol,* 71**,** 1-5.

GRANT, B. F. & DAWSON, D. A. 1997. Age at onset of alcohol use and its association with DSM-IV alcohol abuse and dependence: results from the National Longitudinal Alcohol Epidemiologic Survey. *J Subst Abuse,* 9**,** 103-10.

GROENMAN, A. P., JANSSEN, T. W. P. & OOSTERLAAN, J. 2017. Childhood Psychiatric Disorders as Risk Factor for Subsequent Substance Abuse: A Meta-Analysis. *Journal of the American Academy of Child & Adolescent Psychiatry,* 56**,** 556-569.

GUTTMANNOVA, K., BAILEY, J. A., HILL, K. G., LEE, J. O., HAWKINS, J. D., WOODS, M. L. & CATALANO, R. F. 2011. Sensitive periods for adolescent alcohol use initiation: predicting the lifetime occurrence and chronicity of alcohol problems in adulthood. *J Stud Alcohol Drugs,* 72**,** 221-31.

HAGLER, D. J., JR., HATTON, S., CORNEJO, M. D., MAKOWSKI, C., FAIR, D. A., DICK, A. S., SUTHERLAND, M. T., CASEY, B. J., BARCH, D. M., HARMS, M. P., WATTS, R., BJORK, J. M., GARAVAN, H. P., HILMER, L., PUNG, C. J., SICAT, C. S., KUPERMAN, J., BARTSCH, H., XUE, F., HEITZEG, M. M., LAIRD, A. R., TRINH, T. T., GONZALEZ, R., TAPERT, S. F., RIEDEL, M. C., SQUEGLIA, L. M., HYDE, L. W., ROSENBERG, M. D., EARL, E. A., HOWLETT, K. D., BAKER, F. C., SOULES, M., DIAZ, J., DE LEON, O. R., THOMPSON, W. K., NEALE, M. C., HERTING, M., SOWELL, E. R., ALVAREZ, R. P., HAWES, S. W., SANCHEZ, M., BODURKA, J., BRESLIN, F. J., MORRIS, A. S., PAULUS, M. P., SIMMONS, W. K., POLIMENI, J. R., VAN DER KOUWE, A., NENCKA, A. S., GRAY, K. M., PIERPAOLI, C., MATOCHIK, J. A., NORONHA, A., AKLIN, W. M., CONWAY, K., GLANTZ, M., HOFFMAN, E., LITTLE, R., LOPEZ, M., PARIYADATH, V., WEISS, S. R., WOLFF-HUGHES, D. L., DELCARMEN-WIGGINS, R., FELDSTEIN EWING, S. W., MIRANDA-DOMINGUEZ, O., NAGEL, B. J., PERRONE, A. J., STURGEON, D. T., GOLDSTONE, A., PFEFFERBAUM, A., POHL, K. M., PROUTY, D., UBAN, K., BOOKHEIMER, S. Y., DAPRETTO, M., GALVAN, A., BAGOT, K., GIEDD, J., INFANTE, M. A., JACOBUS, J., PATRICK, K., SHILLING, P. D., DESIKAN, R., LI, Y., SUGRUE, L., BANICH, M. T., FRIEDMAN, N., HEWITT, J. K., HOPFER, C., SAKAI, J., TANABE, J., COTTLER, L. B., NIXON, S. J., CHANG, L., CLOAK, C., ERNST,

T., REEVES, G., KENNEDY, D. N., HEERINGA, S., PELTIER, S., et al. 2019. Image processing and analysis methods for the Adolescent Brain Cognitive Development Study. *Neuroimage,* 202**,** 116091.

HANNIGAN, J. H., CHIODO, L. M., SOKOL, R. J., JANISSE, J. & DELANEY-BLACK, V. 2015. Prenatal alcohol exposure selectively enhances young adult perceived pleasantness of alcohol odors. *Physiology & behavior,* 148**,** 71-77.

JACKSON, K. M., BARNETT, N. P., COLBY, S. M. & ROGERS, M. L. 2015. The Prospective Association Between Sipping Alcohol by the Sixth Grade and Later Substance Use. *Journal of Studies on Alcohol and Drugs,* 76**,** 212-221.

KESSLER, R. C., AVENEVOLI, S., GREEN, J., GRUBER, M. J., GUYER, M., HE, Y., JIN, R., KAUFMAN, J., SAMPSON, N. A., ZASLAVSKY, A. M. & MERIKANGAS, K. R. 2009. National Comorbidity Survey Replication Adolescent Supplement (NCS-A): III. Concordance of DSM-IV/CIDI Diagnoses With Clinical Reassessments. *Journal of the American Academy of Child & Adolescent Psychiatry,* 48**,** 386-399.

LEES, B., MEWTON, L., JACOBUS, J., VALADEZ, E., STAPINSKI, L. A., TEESSON, M., TAPERT, S. F. & SQUEGLIA, L. M. in press. Association of Prenatal Alcohol Exposure With Psychological, Behavioral, and Neurodevelopmental Outcomes in Children From the Adolescent Brain Cognitive Development Study. *Am J Psychiatry*.

LEES, B., MEWTON, L., STAPINSKI, L. A., SQUEGLIA, L. M., RAE, C. D. & TEESSON, M. 2019. Neurobiological and cognitive profile of young binge drinkers: A systematic review and meta-analysis. *Neuropsychology Review,* 29**,** 357-385.

MEQUE, I., DACHEW, B. A., MARAVILLA, J. C., SALOM, C. & ALATI, R. 2019. Externalizing and internalizing symptoms in childhood and adolescence and the risk of alcohol use disorders in young adulthood: A meta-analysis of longitudinal studies. *Australian & New Zealand Journal of Psychiatry,* 53**,** 965-975.

MERIKANGAS, K., AVENEVOLI, S., COSTELLO, J., KORETZ, D. & KESSLER, R. C. 2009. National comorbidity survey replication adolescent supplement (NCS-A): I. Background and measures. *J Am Acad Child Adolesc Psychiatry,* 48**,** 367-9.

O'LEARY, C. M., BOWER, C., ZUBRICK, S. R., GEELHOED, E., KURINCZUK, J. J. & NASSAR, N. 2010. A new method of prenatal alcohol classification accounting for dose, pattern and timing of exposure: improving our ability to examine fetal effects from low to moderate alcohol. *J Epidemiol Community Health,* 64**,** 956-62.

POPOVA, S., LANGE, S., PROBST, C., GMEL, G. & REHM, J. 2017. Estimation of national, regional, and global prevalence of alcohol use during pregnancy and fetal alcohol syndrome: a systematic review and meta-analysis. *The Lancet Global Health,* 5**,** e290-e299.

SIMONS-MORTON, B., HAYNIE, D. L., CRUMP, A. D., EITEL, S. P. & SAYLOR, K. E. 2001. Peer and parent influences on smoking and drinking among early adolescents. *Health Educ Behav,* 28**,** 95-107.

Figure caption. Associations between prenatal alcohol exposure (PAE) and endorsement of alcohol sipping by age 9 to 10 years*.

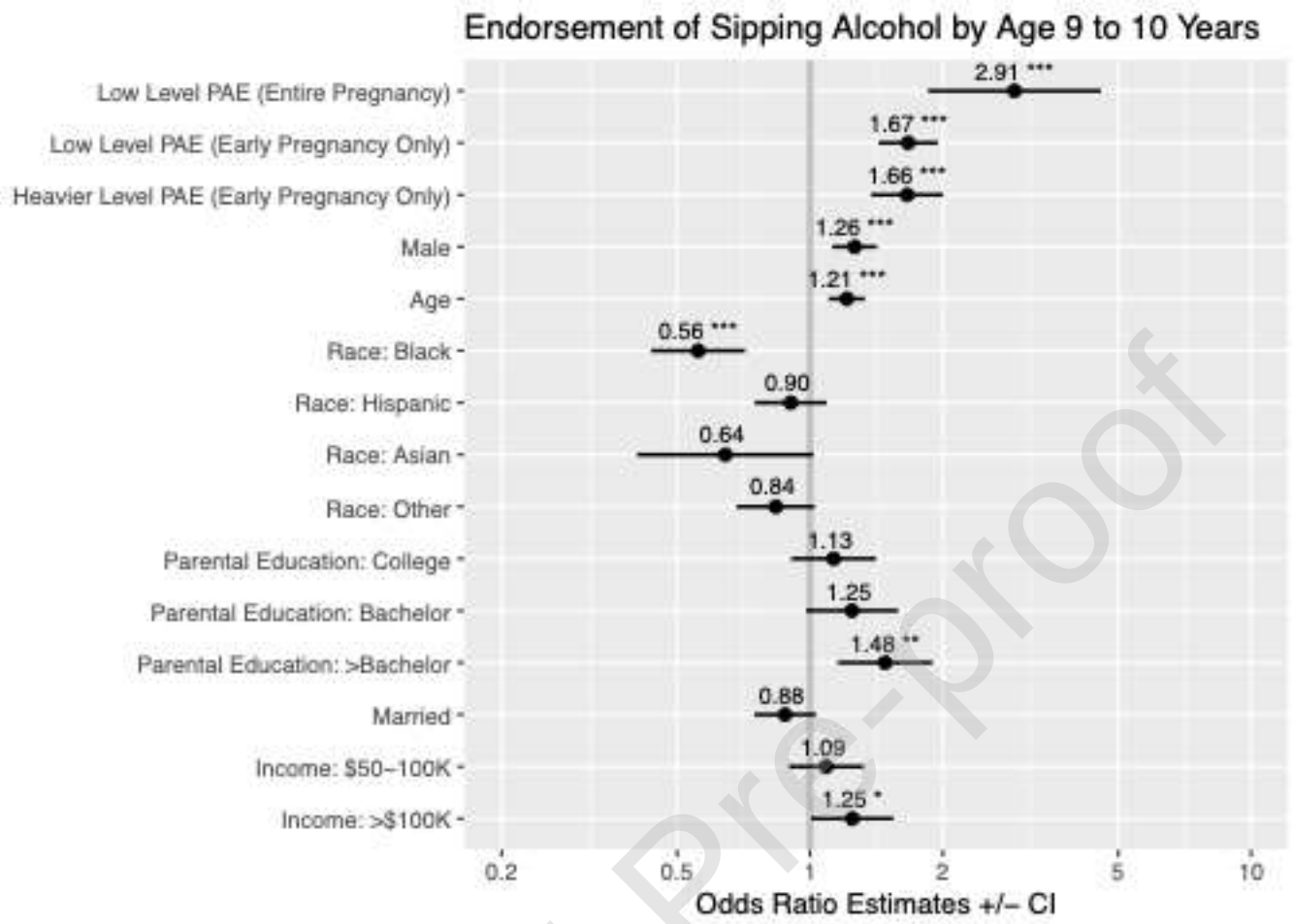


***Figure footnotes.** Odds ratio estimates with 95% confidence intervals are presented. Reference categories for each variable: PAE = unexposed youth; sex = female; race = White; parent education = high school; marital status = single-parent household; income = <$50K.

Table. Characteristics of unexposed and prenatally alcohol exposed youth (n=10,119).

	Unexposed youth	**Prenatally exposed youth**	***p***
Overall, No. (%)	7444 (73.6)	2675 (26.4)	
Male, No. (%)	3899 (52.4)	1366 (51.1)	.25
Age, mean (SD)	9.9 (0.6)	9.9 (0.6)	.73
White, No. (%)	3795 (51.0)	1720 (64.3)	<.001
Parent ≥Bachelor education, No. (%)	3790 (50.9)	1723 (64.5)	<.001
Married/defacto, No. (%)	5525 (74.2)	2009 (75.1)	.38
Household income >100k, No. (%)	2774 (37.3)	1362 (50.9)	<.001
Tobacco use during pregnancy, No. (%)	677 (9.1)	667 (24.9)	<.001
Cannabis use during pregnancy, No. (%)	223 (3.0)	349 (13.1)	<.001
Cocaine use during pregnancy, No. (%)	10 (0.1)	49 (1.8)	<.001
Heroin use during pregnancy, No. (%)	8 (0.1)	8 (0.3)	<.001
Parent history of alcohol problems, No. (%)	892 (12.0)	520 (19.4)	<.001
Lifetime sipping endorsement, No. (%)	1059 (14.2)	686 (25.7)	<.001
	No. (%)	**Mean drinks (SD)**	
Total alcohol use, mean (SD)*		26.8 (24.5)	
Low-level use during early pregnancy	1285 (48.0)	16.1 (18.8)	
Heavier-level use during early pregnancy	803 (30.0)	47.8 (76.3)	
Low-level use throughout pregnancy	95 (3.6)	49.0 (35.9)	

***Table footnotes.** Due to missing data for alcohol use patterns, % does not equate to 100. Mean drinks are calculated from the sub-sample who consumed alcohol during pregnancy.